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Critical Care [ALERT]

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Authoritative, evidence-based summaries for the critical care clinician

ABSTRACT & COMMENTARY

Reducing Daily Chest Radiographs in the ICU

By Samuel Nadler, MD, PhD

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Dr. Nadler reports no relationships relevant to this field of study.

SYNOPSIS: Quality improvement protocols can reduce the number of chest radiographs in the ICU without compromising care.

SOURCE: Sy E, et al. Implementation of a quality improvement initiative to reduce daily chest radiographs in the intensive care unit. *BMJ Qual Saf* 2015 Sept 8 [Epub ahead of print].

Routine, daily chest radiographs (CXRs) are often ordered on all patients in the ICU, particularly on mechanically ventilated patients. However, several studies have called into question the utility of this practice. In 2003, Krivopal et al randomized patients to routine vs non-routine CXR and demonstrated no difference in duration of mechanical ventilation, ICU length of stay (LOS), and total LOS despite a 36% reduction in the number of radiographs in the non-routine group.[1] Graat et al performed a prospective, non-randomized study requiring a clinical indication and new order for radiographs.[2] The number of studies dropped by 56% without a change in length of ICU stay, ICU readmission, and hospital mortality.[2] A 2010 meta-analysis included these studies, demonstrating that elimination of routine CXRs had no effect on hospital or ICU mortality.[3] More recently, the American College of Radiology changed its recommendations to state that CXRs should be ordered "for clinical indications only," even in mechanically ventilated patients.[4] However, ICUs continue ordering millions of routine CXRs.

This study is a before-after design that sought to reduce the number of routine CXRs in the ICU. Between June 2014 and 2015, data were collected as the pre-intervention baseline in a 350-bed, tertiary, teaching hospital with a 15-bed mixed medical-surgical ICU. Patients with trauma, thoracic surgery,

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neurosurgery, or liver/lung transplants were excluded. The interventions to change practices included education of the house staff at the beginning of each month and a prompt within the computerized order entry system that required an acceptable indication to order a CXR. Overall, 1492 patients were enrolled, 738 in the pre-intervention group and 754 in the post-intervention group, with a mean age of 58 and 59 years, respectively. The two groups were well matched for APACHE II (22 vs 21), ICU mortality (20% vs 19%), hospital mortality (31% vs 26%), ICU LOS (6 vs 5 days), and days of mechanical ventilation (1.3 vs 1.4 days). Prior to the intervention, 0.73 CXRs per patient-day were ordered compared with 0.54 afterward, a 26% reduction. There was no significant increase in urgent CXRs performed (post/pre ratio 1.03; 95% confidence interval [CI], 0.91-1.15), although there was a modest increase in stat CXRs (post/pre ratio 1.18; 95% CI, 1.05-1.30). There were no changes in the number of chest CTs ordered, lines or intubations, days of mechanical ventilation, ICU LOS, ICU mortality, or hospital mortality.

■ COMMENTARY

This study presents a practical, real-world protocol that was effective in reducing daily CXRs in a mixed medical-surgical ICU without obvious adverse effects. In the 1-year intervention period, the protocol prevented 1086 CXRs in this 15-bed ICU, and the institution continues this protocol. The cost savings were estimated at CA$27,150 and would likely be far greater in many clinical settings. The intervention included regular education to house staff and an easily generalizable prompt within the electronic medical record for ordering CXRs. The acceptable indications for CXRs were: unexplained new cardiopulmonary symptoms or signs, suspected new pneumonia, suspected new pneumothorax, suspected new pleural effusion, insertion of endotracheal tubes/central venous catheters/chest tubes, suspected malposition of existing tubes, and an "other" category.

This study raises several questions that deserve further consideration. There was a statistically significant increase in stat CXRs, but this increase did not affect mortality or LOS. Data were presented regarding the number of CXRs per patient-day on a weekly basis and demonstrated a significant degree of variability (0.5-1 pre-intervention and 0.3-0.8 post-intervention). This suggests that despite more standardized criteria for CXRs, large practice variations persist. As residents are learning not to order routine CXRs, the need for protocols to reduce these studies may become less frequent. Additionally, the indications mandated for CXRs in this protocol include pleural effusion and pneumothorax. Both may be better evaluated by bedside ultrasonography, which more recent trainees are using with greater frequency.

[This study presents a practical, real-world protocol that was effective in reducing daily CXRs in a mixed medical-surgical ICU without obvious adverse effects.]

Overall, this study shows the efficacy of a simple, generalizable quality improvement project to reduce unnecessary routine CXRs in the ICU that realizes significant cost savings without compromising clinical care. ■

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ABSTRACT & COMMENTARY

Is Less More or More Less? Oxygen Saturation Goals in the Mechanically Ventilated

By Eric C. Walter, MD, MSc

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Dr. Walter reports no financial relationships relevant to this field of study.

SYNOPSIS: A pilot study suggests that a conservative oxygenation approach in patients on mechanical ventilation is feasible and may not have adverse consequences.

SOURCE: Panwar R, et al. Conservative versus liberal oxygenation targets for mechanically ventilated patients — a pilot multicenter randomized controlled trial. *Am J Respir Crit Care Med* 2015 Sept 3 [Epub ahead of print].

Supplemental oxygen is almost universally provided to patients requiring mechanical ventilation, usually to correct some degree of hypoxia. However, there are little data to guide clinicians in determining oxygen saturation goals and the amount of oxygen needed to achieve these goals. With too little oxygen, hypoxia and tissue ischemia are obvious concerns, but there are also increasing concerns about the risks of hyperoxia.

The primary goal of this multicenter, randomized, controlled trial was to determine if it was feasible to perform a randomized controlled study comparing a conservative oxygen therapy strategy (goal pulse oximeter measured saturation [SpO_2] of 88-92%) and a liberal oxygen therapy strategy (goal $SpO_2 \geq$ 96%). Secondary outcomes included hypoxia (defined as $SpO_2 < 88\%$), measures of organ dysfunction (duration of mechanical ventilation, vasopressor use, serum creatinine, etc.), length of stay, and mortality. Positive end-expiratory pressure (PEEP) was determined by the treating clinicians.

Results showed it was feasible to demonstrate a separation in SpO_2 between the two groups. The mean SpO_2 in the conservative group was 93% vs 97% in the liberal group ($P < 0.001$). Mean partial pressure of arterial oxygen (PaO_2) also significantly differed: 70 mmHg in the conservative group vs 92 mmHg in the liberal group ($P < 0.001$). PEEP levels did not differ between groups. Hypoxia was quite rare (1% and 0.3% of time in the conservative and liberal groups, respectively). On the other hand, there was evidence that oxygen was used excessively. Despite having an $SpO_2 > 98\%$, patients were receiving supplemental oxygen ($FiO_2 > 0.21$) 22% of the time. There were no other significant differences in any of the measures of organ dysfunction, length of stay, or mortality.

■ COMMENTARY

The optimal oxygenation target among mechanically ventilated patients is not known. Clearly, we wish to avoid hypoxia, but defining a safe cutoff for hypoxia is challenging. In the landmark acute respiratory distress syndrome network (ARDSNet) low tidal volume study, the goal SpO_2 range was 88-95%.[1] However, some are beginning to question whether this range is too low and whether mild hypoxemia could be related to the observed poor long-term neurocognitive outcomes of some ICU survivors. Conversely, hyperoxia has been associated with increased mortality in post-cardiac arrest, stroke, and traumatic brain injury patients.[2]

With these questions in mind, Panwar et al sought to determine if it would be feasible to conduct a study comparing conservative and liberal oxygenation strategies. The authors show this is possible. They were clearly able to show a difference in mean SpO_2 between the two groups over the course of an entire ICU. The difference between a mean SpO_2 of 93% and 97% is of uncertain clinical significance in any individual patient. However, that was not the objective of the study.

Beyond showing feasibility, the authors reported no evidence of harm with either the conservative or liberal strategy. This is reassuring, but the study was not powered for these outcomes, and this study does not rule out the potential for harm. The rarity of hypoxia was quite striking, especially in the conservative arm where the target SpO_2 range was 88-92%. It should be noted that these patients were not overly sick. At the time of enrollment, only 33% of the conservative oxygen group and 20% of the liberal oxygen group had ARDS, and the mean PaO_2/FiO_2 was approximately 250 in both groups. It is doubtful that

hypoxic episodes would have been so rare if patients had more significant ARDS.

A major limitation of this study was that nearly 20% of patients were excluded if their treating clinician felt there was not enough clinical equipoise to enroll a particular patient. This severely limits the generalizability of the study and likely introduced bias. Clinicians may have excluded patients they felt were too sick to be enrolled.

By design, this was a small pilot feasibility study. Given the small size and potential biases, clinicians should be strongly cautioned against using results from this trial to make widespread practice changes. Nevertheless, this study does remind us that oxygen is a treatment to be "prescribed" only when necessary. Frequently, patients receive more supplemental oxygen than needed, and many would do well on less oxygen or even room air. ■

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ABSTRACT & COMMENTARY

Is Optimizing Respiratory Muscle Function During Mechanical Ventilation an Illusion?

By Richard Kallet, MS, RRT, FAARC, FCCM

Director of Quality Assurance, Respiratory Care Services, San Francisco General Hospital

Mr. Kallet reports no financial relationships relevant to this field of study.

SYNOPSIS: Rapid loss in diaphragmatic thickness during the first week of mechanical ventilation is common and associated with higher levels of ventilator driving pressure.

SOURCE: Goligher EC, et al. Evolution of diaphragm thickness during mechanical ventilation: Impact of inspiratory effort. *Am J Respir Crit Care Med* 2015 Jul 13 [Epub ahead of print].

Goligher et al conducted a multicenter trial using daily transthoracic ultrasonography to measure diaphragmatic contractile activity and thickness in 107 critically ill patients with the goal of assessing whether these measurements were affected by the level of inspiratory effort during mechanical ventilation (MV). The trial explored the evolution of diaphragm thickness over time, the impact of diaphragmatic contractile activity on diaphragm thickness, and the role of MV, including ventilator mode and driving pressure (a signifier for ventilator work output) on diaphragmatic contractile activity. Changes in muscle thickness > 10% from baseline in either direction were deemed clinically meaningful.

Diaphragmatic activity varied widely between patients and within individual patients over time. In the first week of MV, 44% of patients had no change in diaphragm thickness, 44% had evidence of clinically significant decreases in diaphragm thickness, and 12% had a significant increase in thickness. Most changes occurred within days of initiating MV. Loss of diaphragmatic thickness did not differ between patients who were ventilated with assist-control or partial support modes. Lower diaphragmatic contractile activity was associated with decreasing diaphragm thickness over time and higher activity with increasing thickness, although this was most pronounced during the first week of MV. Higher daily Sequential Organ Failure Assessment (SOFA) scores also were associated with increased diaphragm thickness, having an additive effect to diaphragmatic contractile activity. Significant inverse relationships were discovered between diaphragm thickness and diaphragmatic contractile activity with ventilator driving pressures; lower driving pressures and partially assisted modes of MV were associated with higher diaphragmatic contractile activity. Most importantly, both reduced and increased diaphragmatic thickness was associated with dysfunction. This suggests that increased thickness likely signifies muscle inflammation and structural injury from excessive inspiratory workloads rather than hypertrophy. No other baseline characteristics were associated with diaphragmatic thickness.

■ COMMENTARY

This study advances our understanding of the rapidity and variability of respiratory muscle dysfunction in critically ill patients requiring MV. Much of the previous literature has emphasized the problem of "disuse atrophy" during MV, thus indirectly promot-

ing the strategy of "spontaneous breathing" during the entire course of acute respiratory failure. However, this theory neglects the important role of excessive muscular work causing secondary diaphragmatic injury and dysfunction[1] and does not advance our practice of MV during critical illness. Refreshingly, the authors provided a balanced view of this nettlesome problem. That a substantial number of patients showed no ill effects of MV on diaphragmatic function was as important as the fact that approximately three out of every five study subjects had evidence of either rapid loss of muscle mass or injury.

The limitation of this study was its observational nature. The ability to quantify the amount of work sharing between patient and ventilator, the duration of activity, and the underlying source of acute respiratory failure (e.g., acute exacerbation of chronic obstructive lung disease vs acute lung injury) are crucial details needed to improve patient management. Future studies should perform ultrasonic measurements of diaphragmatic activity and thickness when both the degree of inspiratory support provided and inspiratory muscle pressure generated can be reasonably controlled. Moreover, measurements of diaphragmatic electromyography and inflammatory mediators would be helpful in further elucidating the mechanisms promoting diaphragmatic dysfunction from both excessive and insufficient stimulation.

An overlooked aspect of this problem is that modern MV began with the birth of the ICU in the mid-1960s, approximately 10 years before intense research into respiratory muscle function began. Thus, the nature of respiratory muscle dysfunction resulting from critical illness and prolonged MV was not well understood. This lack of knowledge leads to a bias toward overemphasizing disuse atrophy and promoting partial MV support early in the course of critical illness. This has probably been detrimental to hypotensive patients, particularly those with severe infection or trauma, and has likely promoted respiratory muscle injury contributing to prolonged dysfunction and ventilator dependence.

On the other hand, those of us who have focused on measuring patient work of breathing (WOB) during MV may have inadvertently promoted the opposite problem. It's highly unlikely that the evolutionary success of mammals could have occurred without the ability to at least double normal WOB levels for extended periods of time without significant consequences. What became apparent as my own research experience matured (particularly with the advent of lung-protective ventilation) was that MV did not necessarily normalize WOB, so much as sufficiently enhance minute ventilation to levels required by critical illness despite their increased workload. Putting this issue into perspective, approximately 75% of critically ill patients are not ventilator-dependent once they reach the recovery phase.[2] Nonetheless, there is ample room to enhance our understanding of the interplay between MV and respiratory muscle function. This will undoubtedly improve our care, regardless of whether "optimization" is a realistic achievement for all patients requiring MV. ■

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ABSTRACT & COMMENTARY

Nutrition in the ICU: The Controversy Continues

By Kathryn Radigan, MD

Assistant Professor, Pulmonary Medicine, Northwestern University, Feinberg School of Medicine, Chicago

Dr. Radigan reports no financial relationships relevant to this field of study.

SYNOPSIS: When comparing critically ill patients who receive standard enteral feeding vs permissive underfeeding, there is no difference in 90-day mortality.

SOURCE: Arabi YM, et al. Permissive underfeeding or standard enteral feeding in critically ill adults. *N Engl J Med* 2015;372:2398-2408.

Arabi et al sought to compare an enteral feeding plan that included permissive underfeeding (restriction of non-protein calories) vs standard enteral feeding in critically ill patients. In this unblinded, randomized, controlled trial conducted at seven tertiary care centers in Saudi Arabia and Canada between November 2009 and September 2014, 894 critically ill patients were randomized to permissive underfeeding (40-60% of calculated caloric requirements) or standard enteral feeding (70-100% caloric

requirements) for up to 14 days while maintaining the full recommended amount of protein. The primary outcome was 90-day mortality.

The permissive-underfeeding group received fewer mean calories than did the standard-feeding group (835 ± 297 kcal per day vs 1299 ± 467 kcal per day, $P < 0.001$; 46% ± 14% vs 71% ± 22% of caloric requirements, $P < 0.001$) with similar protein intake. For the primary outcome, 121 of the 445 patients (27.2%) in the permissive-underfeeding group and 127 of 440 patients (28.9%) in the standard-feeding group died (relative risk, 0.94; 95% confidence interval, 0.76-1.16; $P = 0.58$). There were no significant differences between groups with respect to intolerance of feeds, diarrhea, infections, ICU length of stay (LOS), or hospital LOS. The investigators concluded that there was no difference in mortality between patients fed with standard enteral feeding vs permissive underfeeding.

[With the intense focus on calories, protein, and other details, it is possible that the effect of timing beyond early vs late has been overlooked. Establishing optimal feeding protocols that prevent muscle dysfunction is crucial as we continue to expand our knowledge of nutritional support strategies in the ICU.]

■ COMMENTARY

Critically ill patients are usually unable to eat by mouth for prolonged periods of time, which can contribute to the poor outcomes associated with critical illness. Multiple studies have explored issues surrounding nutritional support for critically ill patients, comparing trophic vs full enteral feeding, continuous intravenous vs enteral feeding, and timing of feeding. These studies have contributed to our growing, but still limited, knowledge on the ideal nutritional strategy in the ICU. Arabi et al were able to show there was no difference in outcomes for patients who were fed with standard enteral feeding vs permissive underfeeding. These results are similar to two other randomized, controlled trials that evaluated minimal or trophic feeding in patients with acute lung injury or respiratory failure.[1,2] Arabi et al note that their trial was different from the two previously published studies in several ways: 1) the degree of caloric restriction was more moderate, but the duration was more prolonged, 2) supplemental protein was given to the permissive-underfeeding group, 3) enteral fluids were administered to minimize differences in enteral feeding, and 4) calories were estimated as total calories (not non-protein calories). Although the researchers hypothesized that a permissive-underfeeding strategy that restricts non-protein calories but preserves protein intake may provide benefit, the evidence suggests there is no difference in outcomes.

To confuse the issue further, some studies have shown that underfeeding in the first ICU week may have some beneficial effects.[3,4] Interestingly, the trials that suggest no benefit of reaching calorie goals in the first week of ICU stay often include younger patients. This finding serves as a reminder that critically ill patients within any ICU are a heterogeneous group. Rather than a "one prescription for all" approach, the art of medicine must be applied. Furthermore, we may need to address these questions with a different approach. With no data to support the practice, most critically ill patients are fed on a 24-hour continuous protocol. This practice ignores the natural clocks that allow organisms to anticipate cycles of feeding, activity, and rest — the biologic basis for circadian "hunger." There are animal models to suggest that feedings out of sync with the metabolic clock in muscle may be ineffective or harmful.[5] With the intense focus on calories, protein, and other details, it is possible that the effect of timing beyond early (before 48 hours) vs late has been overlooked. Establishing optimal feeding protocols that prevent muscle dysfunction is crucial as we continue to expand our knowledge of nutritional support strategies in the ICU. ■

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ABSTRACT & COMMENTARY

Does Atrial Fibrillation Portend a Worse Prognosis in the ICU?

By Betty Tran, MD, MSc, Editor

SYNOPSIS: In this prospective, observational cohort study, both new-onset and recurrent atrial fibrillation were associated with increased hospital mortality, especially in patients without sepsis.

SOURCE: Shaver CM, et al. Atrial fibrillation is an independent predictor of mortality in critically ill patients. *Crit Care Med* 2015;43:2104-2111.

In this prospective, observational study from Vanderbilt University Medical Center, 1770 critically ill adults (1275 medical ICU and 495 surgical ICU patients) were followed to test the hypothesis that atrial fibrillation (AF) during critical illness was associated with increased hospital mortality independent of severity of illness and comorbidities. The authors also examined whether there were differences in risk factors and outcomes in patients with new-onset AF vs recurrent AF and in patients with sepsis and non-sepsis, and whether variables such as a more positive fluid balance, higher vasopressor requirement, and prior cardiac disease were associated with an increased risk of AF.

Overall, 236 patients developed AF during the 4-day study period in the ICU, with 123 of these categorized as new-onset AF and 113 experiencing recurrent AF. Compared to recurrent AF patients, those with new-onset AF tended to have more organ failure and shock, whereas recurrent AF patients were more likely to have a history of congestive heart failure, hypertension, and hyperlipidemia. After controlling for potential confounders such as age, cardiac history, APACHE II score, shock, and sepsis, development of any AF was associated with a 62% increased risk of hospital mortality (95% confidence interval [CI], 1.14-2.29; $P = 0.007$). This association occurred for both new-onset and recurrent AF, separately. Patients with any AF also had significantly longer ICU and hospital lengths of stay. Compared to patients with no AF or recurrent AF, new-onset AF patients had significantly greater net positive cumulative fluid balance (median 6.1 L vs 5.4 L; $P = 0.034$), more frequently had diastolic dysfunction, were more likely to be treated with vasopressors, and were on vasopressors longer. Although an occurrence of any AF was associated with increased hospital mortality regardless of the presence of sepsis, the association was magnified in patients without sepsis (odds ratio, 2.92; 95% CI, 1.52-5.60; $P = 0.001$).

■ COMMENTARY

AF commonly occurs in the ICU and is often difficult to manage, especially in the setting of hypotension. The study by Shaver et al suggests that its presence may have more significant implications. There are several strengths to this study, including the large sample size of mixed medical and surgical ICU patients and the ability to distinguish between new and recurrent AF. Although the authors included APACHE II score and the presence of shock and sepsis in their multivariable regression models in an attempt to control for AF being a mere marker of severe illness, it is possible there is still residual confounding present. Intuitively, it makes sense that patients with new-onset AF are usually sicker than non-AF patients; in the study, AF patients had higher APACHE II scores, more organ failures, higher cumulative fluid balance, and more frequent and/or longer need for vasopressors (implying more severe hypotension or hypotension of longer duration). Additionally, recurrent AF patients often have traditional cardiac comorbidities such as congestive heart failure, hypertension, and hyperlipidemia.

Although severity of illness is likely a contributor, the exact relationship between AF and mortality is still unclear. As suggested by the authors in citing a "two-hit" model for development of AF, patients who develop AF may have a genetic propensity to develop it in response to triggers commonly seen in critical illness. Given the interest in exploring genetics in sepsis, could there be an overlap in genetic risk for development of AF and sepsis, especially a more severe systemic inflammatory response? Or is development of AF in critically ill patients just less well-tolerated? Additional studies aimed toward treating AF and preventing it with a focus on patient outcomes will be enlightening. ■

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CME/CNE QUESTIONS

1. Elimination of routine daily chest radiographs in the ICU has been shown to do which of the following?
a. Decrease cost of care
b. Increase ICU length of stay
c. Decrease ICU mortality
d. Increase hospital length of stay
e. All of the above

2. With respect to the study by Panwar et al comparing a conservative and liberal oxygenation strategy, which of the following statements is/are true?
a. In the liberal oxygenation group, patients received excess oxygen.
b. Using a conservative oxygenation strategy requires significantly higher positive end-expiratory pressure.
c. It was feasible to demonstrate a separation in SpO_2 between the two groups.
d. The authors were able to definitively conclude that the use of a conservative oxygenation strategy is not harmful.
e. Both a and c

3. Which of the following is false regarding respiratory muscle function and mechanical ventilation?
a. Completely passive ventilation leads to "disuse" muscle atrophy.
b. Excessive loading promotes diaphragmatic injury and inflammation.
c. Approximately 75% of critically ill patients are ventilator-dependent.
d. A sizable minority (approximately 40%) of patients do not manifest signs of diaphragmatic dysfunction as a result of mechanical ventilation.
e. Both a and c

4. When comparing permissive enteral underfeeding vs standard enteral feeding in critically ill patients, there was no significant difference in:
a. 90-day mortality.
b. ICU length of stay.
c. hospital length of stay.
d. feeding intolerance.
e. All of the above

5. In the study by Shaver et al, atrial fibrillation in critically ill patients was associated with:
a. longer ICU length of stay.
b. longer hospital length of stay.
c. higher hospital mortality.
d. All of the above
e. None of the above

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Upon completion of this educational activity, participants should be able to:

- identify the particular clinical, legal, or scientific issues related to critical care;
- describe how those issues affect physicians, nurses, health care workers, hospitals, or the health care industry; and
- cite solutions to the problems associated with those issues.

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